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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,874	08/20/2003	Kenneth F. Buechler	071949-7002	8658

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FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
LUM, LEON YUN BON	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,874	BUECHLER ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1-28 and 34-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/12/03, 11/24/04, 1/24/05, 9/1/05, 9/6/05, 12/8/05, 1/19/06, 4/24/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed July 6, 2006 is acknowledged and has been entered.

Election/Restrictions

2. Applicant's election without traverse of Group II, claims 29-33 in the reply filed on July 6, 2006 is acknowledged.

Priority

3. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 10/419,059, 09/835,298, 10/139,086, 60/288,871, 60/315,642, PCT/US02/26604, 60/313,775, 60/334,964, and 60/346,485, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The prior-filed applications disclose natriuretic peptides and detection

methods thereof. However, the prior-filed applications fail to disclose the step of administering prolyl-specific DPP inhibitors in an amount sufficient to inhibit natriuretic peptide degradation. In fact, the terms DPP and dipeptidyl peptidase, and specific inhibitors thereof, are not mentioned in the prior-filed applications.

Information Disclosure Statement

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining

compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

For example, Applicants filed a "Notice of References Cited" form PTO-892 on January 24, 2005. The document also fails to include the proper Application number as required under 37 CFR 1.98.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 29-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims include the limitation "[A]dministering one or more inhibitors of prolyl-specific DPP in an amount ***sufficient*** to inhibit degradation of the natriuretic peptide." See claim 29, lines 3-4 and claim 32, lines 2-3. None of the instant claims provides an amount of inhibitor that would lend one of ordinary skill in the art to recognize as "sufficient" in preventing degradation of natriuretic peptide. In consulting the specification, it is determined that sections 0073-0074, 0126-0128, and 0135-0136

are relevant to the claims. However, none of these sections provides an adequate description of prolyl-specific DPP inhibitors that meets the claim limitation. For example, section 0074 (pages 23-24) defines the term "inhibitor" as a molecule that reduces an enzymatic activity by a range from at least 10% to at least 90% of the enzymatic activity exhibited in the absence of the inhibitor. However, this section does not disclose a specific amount of inhibitor, or even identify a specific inhibitor, that is deemed "sufficient" to inhibit natriuretic peptide degradation.

In section 0127, specific DPP inhibitors are disclosed with reference to numerous publications. However, the specification does not link a specific amount with the said inhibitors that would be "sufficient" to inhibit natriuretic peptide degradation. Even the combination of both sections 0074 and 0127 fails to provide adequate support for an amount of each DPP inhibitor disclosed since the percentages in section 0074 are given in relative terms and not specific amounts.

In section 0136, actual amounts of 0.001 mg/kg per day to 1000 mg/kg per day are disclosed as being "effective amounts". However, these amounts are not directed towards specific DPP inhibitors and are presented in general terms. The section even states that "The effective amount will ***vary*** with the particular condition being treated, the age and physical condition of the subject being treated, the severity of the condition, the duration of the treatment, the nature of the concurrent therapy (if any), the specific route of administration and like factors within the knowledge and expertise of the health practitioner." However, specific amounts of a named inhibitor subject to specific conditions are not disclosed anywhere in the specification. The examples provided on

pages 43-61 do not teach the administering of any amount of DPP inhibitor. Even the combination of sections 0074 (i.e. percentage decrease indicating effective inhibition) and 0127 (i.e. specific DPP inhibitors) with section 0136 (i.e. actual amounts) fails to provide one of ordinary skill with the knowledge to the claimed limitation. With so many factors disclosed as influencing the "effective" amount of dosage, including crucial factors such as the particular condition being treated, a lack of information linking a named inhibitor to a quantified amount prevents one of ordinary skill in the art from determining which one of the disclosed dosages in section 0136 to subscribe to which one of the disclosed DPP inhibitors in section 0127.

One of ordinary skill in the art would therefore not recognize that Applicants had possession of the claimed invention due to a lack of written description supporting the above-identified limitation of the instant claims.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 29-30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Meester et al (Biochemical Pharmacology, 1997).

Meester et al teach the step of administering an intravenous injection of Prodipine, an inhibitor of DPP IV (i.e. administering one inhibitor of prolyl-specific DPP). See page 173, abstract; page 174, left column, last paragraph; and page 174, entire right column. In addition, Meester et al teach that the injection of Prodipine produced a prolonged inhibition of plasma DPP IV activity (i.e. sufficient to inhibit degradation of the natriuretic peptide). See page 176, right column and Figures 2-4.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 29, 31, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Bergmann et al (US 6,756,483).

Bergmann et al teach the step of therapeutically blocking dipeptidyl-aminopeptidase IV (DPP IV) by blocking it with suitable binders, antibodies, or similar receptor molecules. See column 3, lines 35-42. Although Bergmann et al do not explicitly teach the claimed administering step or sufficient amount, since the reference teaches the blocking step in a therapeutic situation, it is necessarily required that the binders, antibodies, or receptor molecules be administered *in vivo* in an effective amount.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergmann et al (US 6,756,483) in view of Waeber et al (US 4,839,343).

Bergmann et al reference has been disclosed above, and additionally teaches that the inhibitors are administered to patients suffering from sepsis or sepsis-like inflammation. See column 3, lines 24-42 and 57-60. However, Bergmann et al fail to teach the step of administering one or more additional molecules selected from the group consisting of inhibitors of neutral endopeptidase and natriuretic peptides.

Waeber et al teach the step of administering hexatriacontapeptides, known inducers of natriuresis, but administered in doses too low to cause natriuresis, in order to prevent life-threatening hypotension due to septic shock. See column 2, lines 3-6 and 31-45; and column 3, lines 23-31.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergmann et al to include the step of administering hexatriacontapeptides, as taught by Bergmann et al, in order to prevent life-threatening hypotension due to septic shock. Since Bergmann et al teach that the DPP IV inhibitors are provided to patients having sepsis, the step of administering hexatriacontapeptides would prevent potentially fatal complications while the inhibitors block an underlying cause of sepsis. Motivation is therefore provided in combining Bergmann et al and Waeber et al references. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in combining the references since both Bergmann et al and Waeber et al teach therapeutic steps to treat

the same disease, and Waeber et al teach that additional treatment molecules can be administered concurrently with the hexatricontapeptides. See column 3, lines 40-41.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon Y. Lum
Patent Examiner
Art Unit 1641

LYL

LONG V. LE 07/20/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600